

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference N.78374 DMG/TJD	FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/22045	International filing date (day month/year) 22/09/1999	Priority date (day/month/year) 25/09/1998	
International Patent Classification (IPC) or national classification and IPC C12N15/62			
Applicant REGENERON PHARMACEUTICALS, INC. et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
 - ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- | | | |
|------|-------------------------------------|---|
| I | <input checked="" type="checkbox"/> | Basis of the report |
| II | <input type="checkbox"/> | Priority |
| III | <input type="checkbox"/> | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| IV | <input checked="" type="checkbox"/> | Lack of unity of invention |
| V | <input checked="" type="checkbox"/> | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| VI | <input checked="" type="checkbox"/> | Certain documents cited |
| VII | <input type="checkbox"/> | Certain defects in the international application |
| VIII | <input checked="" type="checkbox"/> | Certain observations on the international application |

Date of submission of the demand 25.02.2000	Date of completion of this report 05.02.2001
Name and mailing address of the international preliminary examining authority  European Patent Office D-80298 Munich Tel: +49 89 2399-10 Fax: +49 89 2399-4465 Fax: +49 89 2399-4465	Authorized officer Vollbach, S Telephone No. +49 89 2399 8715 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US99/22045

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:

Description, pages:

1-72 as originally filed

Claims, No.:

1-25 as originally filed

Drawings, sheets:

1/63-63/63 as originally filed

Sequence listing part of the description, pages:

1-58, filed with the letter of 17.2.00

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

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- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:
5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):
(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:
- ☐ restricted the claims.
☐ paid additional fees.
☒ paid additional fees under protest.
☐ neither restricted nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with.
☒ not complied with for the following reasons:
see separate sheet
4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:
- ☐ all parts.
☒ the parts relating to claims Nos. 1-4,9-25 partially.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N): Yes: Claims 22,24
 No: Claims 1-4,9-21,23,25

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Inventive step (IS)	Yes:	Claims	
	No:	Claims	22,24
Industrial applicability (IA)	Yes:	Claims	1-4,9-21,23,25
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item II

Priority

The present application claims priority from 25.9.1998. The priority document has not been provided and therefore the present authority starts from the assumption that the claimed priority is valid. Should it turn out that this is incorrect, the intermediate documents cited in the search report become relevant for the assessment of patentability of the present application.

Re Item IV

Lack of unity of invention

The applicant was invited to pay additional examination fees or to restrict the claims to one group of invention. In response, two additional examination fees have been paid under protest in accordance with Rule 68.3(c) PCT. The applicant argued that contrary to the view taken by the Search and Examination authority, the concept of the claimed invention is both novel and inventive. Therefore the objection for lack of unity should be set aside and the additional paid examination fees should be refunded.

The present authority, however, takes the view that claim 1 relating to a nucleic acid sequence encoding a fusion protein and claims 12 relating to the fusion protein encoded by the nucleic acid of claim 1 lack novelty over several documents cited in the Search report. As a consequence the present set of claims does no longer fulfil the requirements of Rules 13.1-13.3 PCT.

Therefore the present authority is of the opinion that the non-unity objection is justified. Accordingly an examination will be carried out on the basis of the three selected groups of inventions for which the required fees have been paid.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

I. Claims referring to IL-4 fusion proteins. DNA encoding them and methods for their preparation

D1 (WO 96/11213) discloses dimeric and multimeric IL-4 inhibitors which comprise the soluble IL-4 receptor extracellular domain and the IL-2R γ extracellular domain bound to each other by polymeric spacer molecules such as PEG or Fc. It has been found in said document that the heterodimeric complex is more effective in neutralizing IL-4 bioactivity than sIL-4R. The fusion protein disclosed in D1 contains all the features of claim 12 including the feature that the complex is not functional but binds IL-4.

The same applies with regard to the complex disclosed in D2 (EP-0-835 939) i.e. IL-4R-Fc. It should be noted that due to the word "comprising" used in claim 1, said claim is not restricted to a complex which has only one beta compound.

Therefore claims 1-4, 10-21, 23, and 25 lack novelty over the disclosure of D1 and D2. The use of further host-vector system known in the art for the expression of the fusion protein such as those of claims 22 and 24, cannot render the subject-matter inventive as required by Article 33(2) PCT.

II. Claims referring to IL13 fusion proteins, DNA encoding them and methods for their preparation

D7 (WO 97/31946) discloses IL-13bc-Ig fusion proteins which are useful antagonists for IL3. The extracellular domain was fused to an Ig molecule. This molecule falls meets the definition of claim 1 since it contains all the features mentioned in that claim. Therefore with regard to said disclosure claims 1-4, 10-19 and 25 lack novelty and claims 20-24 cannot positively contribute to inventiveness because the expression systems claimed in claims 20-24 are common to a person skilled in the art. Therefore Articles 33(2) and 33(3) PCT are not fulfilled.

III. Claims relating to IL1 fusion proteins, DNA encoding them and methods for their preparation

D8 (WO93/19777) describes fusion proteins comprising soluble TNF and IL-1 receptors bound to each other by a linker. It is disclosed that these soluble forms of the receptors may also include part of the transmembrane region or the cytoplasmic region. The DNA encoding said receptors are also part of the disclosure of D8.

These receptors are considered to fall within the scope of claims 1-3, 9, 12-21, 23 and 25

are not novel (Article 33(2) PCT). The feature that the multimerizing compound is Fc cannot be regarded to render the claims inventive when combined thereto because it is a well known multimerizing compound. Therefore present claims 10 and 11 are inadmissible under Article 33(3) PCT.

The following objections apply to the present application as a whole:

According to the description, the invention consists in the finding that producing and intermediate complex with only one beta-compound (while two beta subunits are required for signal transduction) results in an antagonist which binds cytokine to form a non functional complex. Apart from the fact that D1 and D6 (WO96/04389) already discloses fusion proteins lacking one beta component, the present authority has some doubts whether this teaching can be applied to any of the listed receptors. In this context emphasis should be put on the large heterogeneity of said receptors.

Re Item VI

Certain documents cited

WO 99 37772 A (BORN TERESA L ;SIMS JOHN E (US); IMMUNEX CORP (US)) 29 July 1999 (1999-07-29)

RE Item VIII

Certain observations on the international application

It should be noted that due to vague definitions used in claim 1, said claim is not restricted to receptors which have been exemplified in The present application (i.e. lacking one beta component). In particular, The wording "non-functional" alone without The indication of The function is unclear and therefore any truncated receptor falls within The scope of The claim because deleting from a receptor parts or domains usually result in The loss of The function attributed to this region. For example deleting The transmembrane region results in The inability to be bound to The membrane. In addition The "multimerizing compound" of item c. of claim 1 can in fact be any amino acid sequence to which e.g. an antibody can be produced which then mediates The multimerization. Finally, due to the word "comprising" claim 1 is not restricted to a receptor having the features set out in item a. to c. of claim 1.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference REG 203-B-PCT	FOR FURTHER ACTION <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. PCT/US 99/ 22045	International filing date (day/month/year) 22/09/1999	(Earliest) Priority Date (day/month/year) 25/09/1998
Applicant REGENERON PHARMACEUTICALS, INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38 2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures

INTERNATIONAL SEARCH REPORT

international application No
PCT/US 99/22045**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons

1. ☐ Claims Nos.
because they relate to subject matter not required to be searched by this Authority, namely
2. ☐ Claims Nos.
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically
3. ☐ Claims Nos.
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6 4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos. :
1-4,9-25 (inventions 1 (IL-2 receptor), 3 (IL-4 receptor), 4 (IL-5 receptor), 7 (IL-9 receptor), 9 (IL-13 receptor), 61 (IL-1 receptor), 65 (IL-18 receptor)
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims, it is covered by claims Nos. .

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest
- ☒ No protest accompanied the payment of additional search fees

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-4,10-25, all partially

Fusion protein, capable of forming a non-functional complex with a cytokine, comprising a specificity-determining component and a signal-transducing component of the IL-2 receptor, and a multimerizing component. Also nucleic acid encoding said fusion protein, (expression) vector comprising said nucleic acid, host cell transformed with said vector, and method for producing said fusion protein using said host.

Inventions 2-66: claims 1-25, all partially,
as far as applicable

As invention 1, but limited to fusion proteins in which the specificity-determining component and the signal-transducing component are derived from the receptors for IL-3, IL-4, IL-5, IL-6, IL-7, IL-9, IL-11, IL-13, IL-15, GM-CSF, OSM, LIF, cardiotrophin-1, IFN-alpha, IFN-beta, IFN-gamma, B7.1/CD80, B7.2/CD86, TNF-alpha, TNF-beta, LT-beta, CD40-L, FAS-L, CD27-L, CD30-L, 4-1BBL, TGF-beta1, TGF-beta2, TGF-beta3, BMP-2, BMP-3a, BMP-3b, BMP-4, BMP-5, BMP-6, BMP-7, BMP-8a, BMP-8b, BMP-9, BMP-10, BMP-11, BMP-15, BMP-16, EBAF, GDF-1, GDF-2, GDF-3, GDF-5, GDF-6, GDF-7, GDF-8, GDF-9, GDF-12, GDF-14, MIS, activin-1, activin-2, activin-3, activin-4, activin-5, IL-1, IL-10, IL-12, IL-14, IL-18, and MIF, whereby invention 2 relates to fusion protein comprising specificity-determining and signal-transducing components from the IL-3 receptor, invention 3 relates to fusion protein comprising specificity-determining and signal-transducing components from the IL-4 receptor,, invention 65 relates to fusion protein comprising specificity-determining and signal-transducing components from the IL-18 receptor, and invention 66 relates to fusion protein comprising specificity-determining and signal-transducing components from the MIF receptor.

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

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International Application No

PCT/US 99/22045

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/62 C07K14/715 C12N15/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, STRAND

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	<p>WO 96 23881 A (CELL GENESYS INC) 8 August 1996 (1996-08-08) page 16, line 14 -page 19, line 25 page 47, line 5 -page 48, line 13 page 51, line 12 -page 52, line 3 page 54, line 31 -page 55, line 17 page 58, line 10 -page 59, line 3 page 61, line 33 -page 62, line 20 page 65, line 10 -page 66, line 3 page 69, line 5 - line 25 page 72, line 4 - line 22 page 75, line 10 -page 76, line 3; claims 1,3,4,6,11,12,14,15,17,23,25,26,ETC...; figure 5</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	1-4,9-25

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

13 July 2000

Date of mailing of the international search report

2000.07.13

Name and mailing address of the ISA

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Authorized officer

Smalt, R

INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED RELEVANT

Category ²	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 94 22914 A (HUTCHINSON FRED CANCER RES ;GREENBERG PHILIP D (US); NELSON BRAD H) 13 October 1994 (1994-10-13) the whole document ---	1-4,9-25
X	WO 96 11213 A (AMGEN BOULDER INC) 18 April 1996 (1996-04-18) cited in the application the whole document ---	1-4,9-25
X	WO 97 15669 A (US HEALTH) 1 May 1997 (1997-05-01) page 18, line 27 - line 34; claims 12,16,28 ---	1-4, 10-25
X	WO 93 19163 A (YEDA RES & DEV) 30 September 1993 (1993-09-30) abstract page 7, line 8 -page 8, line 1 page 8, line 31 - line 36 page 17, line 21 - line 24; claims 1,12,16 ---	1,2,4, 10-25
X	WO 95 06737 A (PRENDERGAST KENNETH FRANCIS) 9 March 1995 (1995-03-09) see seq.ID.16 and the claims ---	1-4, 10-25
X	WO 93 19777 A (IMMUNEX CORP) 14 October 1993 (1993-10-14) claims examples 12,13 ---	1-4, 10-25
X	EP 0 835 939 A (HOECHST AG ;GEN HOSPITAL CORP (US)) 15 April 1998 (1998-04-15) claims 8,9,17,21; example 2 ---	1,2,4, 9-25
X	WO 97 31946 A (GENETICS INST) 4 September 1997 (1997-09-04) claims 11,27,28; example 4 ---	1,2,4, 10-25
X	EP 0 533 006 A (HOFFMANN LA ROCHE) 24 March 1993 (1993-03-24) claims 1,3,5,8-10; examples 12,13 ---	1,2,4, 10-25
X	WO 96 35783 A (DARTMOUTH COLLEGE ;CHIRON CORP (US)) 14 November 1996 (1996-11-14) claims 4,5 ---	1,2,4, 10-25

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	SEIPELT I ET AL: "Overexpression, purification, and use of a soluble human interleukin-4 receptor alpha-chain/Ig gamma 1 fusion protein for ligand binding studies. Characterization of ligand binding to soluble IL-4 receptor alpha-chain by surface plasmon resonance measurements and by microtiter-plate-based ELISA with" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS,US,ACADEMIC PRESS INC. ORLANDO, FL, vol. 239, 20 October 1997 (1997-10-20), pages 534-542, XP002105430 ISSN: 0006-291X the whole document ---	1,2,4, 10-18, 23,25
A	WO 96 04389 A (REGENERON PHARMA) 15 February 1996 (1996-02-15) the whole document ---	
A	WO 97 23613 A (CELLTECH THERAPEUTICS LTD ;BEBBINGTON CHRISTOPHER ROBERT (GB); LAW) 3 July 1997 (1997-07-03) page 5, line 32 -page 6, line 30 page 7, line 26 - line 34; claim 26; figures 14-17 ---	
A	WO 98 02558 A (UNIV MEDICINE AND DENTISTRY OF) 22 January 1998 (1998-01-22) page 8, line 25 -page 10, line 5; figures 1,7,10,17 page 25, line 8 -page 28, line 7; claims 1,7-9 ---	
A	WO 95 10611 A (HARVARD COLLEGE) 20 April 1995 (1995-04-20) claims 5,13; example 1 ---	
A	DUSCHL A ET AL: "TRANSMEMBRANE AND INTRACELLULAR SIGNALLING BY INTERLEUKIN - 4: RECEPTOR DIMERIZATION AND BEYOND" EUROPEAN CYTOKINE NETWORK, 1996, XP002061702 figure 4 ---	
A	EP 0 864 585 A (HAYASHIBARA BIOCHEM LAB) 16 September 1998 (1998-09-16) the whole document ---	
A	WO 93 18047 A (LUDWIG INST CANCER RES) 16 September 1993 (1993-09-16) the whole document ---	

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C.(Continuation) DOCUMENTS CONSIDERED RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
P,X	STAHL, N. ET AL.: "Cytokine traps: heteromeric receptor-based protein therapeutics that function as high-affinity blockers of cytokine action." FASEB JOURNAL, vol. 13, no. 7, 23 April 1999 (1999-04-23), pages A1585-Abstr.1457, XP002133324 the whole document	1-4, 10-14
P,X	--- WO 99 37772 A (BORN TERESA L ;SIMS JOHN E (US); IMMUNEX CORP (US)) 29 July 1999 (1999-07-29) page 3, line 11 - line 26 page 6, line 7 - line 9; examples 1,3,4 page 8, line 22 - line 34 page 10, line 7 - line 15 -----	1-3, 9-18,25

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/22045

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 9623881	A	08-08-1996	AU	715363 B		03-02-2000
			AU	4861296 A		21-08-1996
			CA	2221634 A		08-08-1996
			EP	0821730 A		04-02-1998
			US	5741899 A		21-04-1998
			US	5837544 A		17-11-1998
			US	6077947 A		20-06-2000

WO 9422914	A	13-10-1994	AU	695869 B		27-08-1998
			AU	6627194 A		24-10-1994
			CA	2160011 A		13-10-1994
			EP	0693084 A		24-01-1996
			JP	8511000 T		19-11-1996
			US	5747292 A		05-05-1998

WO 9611213	A	18-04-1996	AU	3830895 A		02-05-1996

WO 9715669	A	01-05-1997	AU	7472496 A		15-05-1997

WO 9319163	A	30-09-1993	AU	3924393 A		21-10-1993
			CA	2132349 A		30-09-1993
			EP	0638119 A		15-02-1995
			JP	7505282 T		15-06-1995

WO 9506737	A	09-03-1995	EP	0716703 A		19-06-1996

WO 9319777	A	14-10-1993	AU	671116 B		15-08-1996
			AU	3970293 A		08-11-1993
			CA	2133326 A		14-10-1993
			EP	0670730 A		13-09-1995
			FI	944516 A		22-11-1994
			JP	7508639 T		28-09-1995
			NO	943617 A		29-11-1994
			NZ	251820 A		26-07-1996
			NZ	280051 A		26-07-1996

EP 0835939	A	15-04-1998	AT	169030 T		15-08-1998
			AU	655421 B		22-12-1994
			AU	7935791 A		02-01-1992
			CA	2045869 A		29-12-1991
			DE	59109032 D		03-09-1998
			EP	0464533 A		08-01-1992
			ES	2120949 T		16-11-1998
			GR	3027567 T		30-11-1998
			JP	5247094 A		24-09-1993
			PT	98113 A,B		29-05-1992

WO 9731946	A	04-09-1997	US	5710023 A		20-01-1998
			AU	1980197 A		16-09-1997

EP 0533006	A	24-03-1993	AU	657788 B		23-03-1995
			AU	2357192 A		25-03-1993
			CA	2078384 A		19-03-1993
			JP	5268967 A		19-10-1993
			NZ	244281 A		27-04-1995
			US	5668256 A		16-09-1997
			US	5712121 A		27-01-1998
			US	5455337 A		03-10-1995

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0533006 A		ZA 9206962 A	13-04-1993
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